

**ZOPICLONE 7.5MG FILM-COATED TABLETS (ZOPICLONE)  
PL 19156/0015**

**UKPAR**

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**ZOPICLONE 7.5MG FILM-COATED TABLETS (ZOPICLONE)  
PL 19156/0015**

**LAY SUMMARY**

The MHRA granted PSI N.V. a Marketing Authorisation (licence) for the medicinal product Zopiclone 7.5mg film-coated tablets (PL 19156/0015) on 15<sup>th</sup> December 2005. This prescription only medicine (POM) is used for the short term treatment of insomnia.

Zopiclone tablets contain the active ingredient zopiclone, which is an hypnotic agent, which rapidly initiates and sustains sleep

The clinical data presented to the MHRA, pre licensing, demonstrated that Zopiclone 7.5mg film-coated tablets are essentially similar or equivalent to the approved products Zimovane 7.5mg tablets. Zopiclone 7.5mg film-coated tablets can therefore be used interchangeably with Zimovane 7.5mg tablets.

No new or unexpected safety concerns arose from these applications and it was, therefore, judged that the benefits of taking Zopiclone 7.5mg film-coated tablets outweigh the risks, hence Marketing Authorisations have been granted.

**ZOPICLONE 7.5MG FILM-COATED TABLETS (ZOPICLONE)  
PL 19156/0015**

**SCIENTIFIC DISCUSSION**

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## **INTRODUCTION**

Based on the review of the data on quality, safety and efficacy the UK granted marketing authorisations for the medicinal products Zopiclone 7.5mg film-coated tablets (PL 19156/0015) to PSI N.V. on 15<sup>th</sup> December 2005. The product is a prescription only medicine.

The application was submitted as an abridged application according to article 10.1(a)(iii) of Directive 2001/83/EC, claiming essential similarity to the original product Zimovane 7.5mg tablets.

The product contains the active ingredient zopiclone and is indicated for the short-term treatment of insomnia.

Zopiclone is an hypnotic agent, and a member of the cyclopyrrolone group of compounds. It rapidly initiates and sustains sleep with reduction of total REM sleep and with preservation of slow wave sleep.

# **PHARMACEUTICAL ASSESSMENT**

## **1. INTRODUCTION**

This is a national complex abridged Marketing Authorisation application for Zopiclone 7.5mg tablets claiming essential similarity in the UK to Zimovane 7.5mg Tablets (PL: 00012/0259 granted 06.05.1993) under EC Article 10.1(a)(iii) of Directive 2001/83/EEC as amended. Hence the 10 year rule is complied with.

The current UK Zimovane 7.5mg Tablet product named above is a gellified product to prevent abuse whereas the original (now withdrawn) Zimovane 7.5mg Tablets granted 23.08.1989 were of conventional immediate release formulation.

Zopiclone tablets are indicated for the short term treatment of insomnia.

## **2. PART IIA – COMPOSITION AND DEVELOPMENT PHARMACEUTICS**

The composition of the film-coated tablet is defined, consisting of the core components of calcium hydrogen phosphate, lactose monohydrate, maize starch, sodium starch glycollate and the lubricant magnesium stearate and the film-coat components. The objective was to produce a tablet comparable to the reference product. During development the effects of disintegrant, binder and lubricant quantities on the final tablet characteristics were investigated before selecting the final formulation for optimisation and scale up.

Satisfactory validation of the dissolution test was provided. The applicant uses the EP paddle method to compare the dissolution of the proposed product with reference products from Belgium, Holland, England, Germany and France.

Comparative impurity data has been supplied for the test product and UK-innovator products.

## **3. PART IIB – METHOD OF PREPARATION**

The manufacturing process is described both in the description and in flow chart form.

Comprehensive in-process controls are exercised. In process control results are given for three batches.

Essential stages of the manufacturing process have been validated using three batches manufactured at the original manufacturing site. Batch analysis data has been provided.

## **4. PART IIC - CONTROL OF STARTING MATERIALS**

Zopiclone is the subject of a PhEur monograph. Two sources were named in the application and certificates of suitability are provided for both. These certificates control any other impurity, with control for boron residual catalyst and control for residual solvents as additional tests. Copies of these certificates of suitability authorise access to the material by the applicant for use in this product. Batch analyses are provided for three batches of Zopiclone. These are in line with the proposed specification. Other ingredients are compendial grade being PhEur. These are supported by certificates of analysis (C of As). The primary packaging consists of PVC/PVdC/aluminium foil blisters. Specifications supported by Certificates of Analysis are provided. Prior to use the starting materials are checked for identity.

## **5. PART IIE – CONTROL TESTS ON THE FINISHED PRODUCTS**

A comprehensive finished product specification is provided for the film coated tablet that includes HPLC assay, identity of Zopiclone by HPLC and TLC and control of related substances. It is stated that test methods are based on pharmacopoeial methods. Test methods specific to the proposed product are provided. Analytical and physico-chemical validation of the UV spectrophotometric method for dissolution and content uniformity has been carried out. The HPLC method for assay and related substance has been validated for various parameters including selectivity, linearity, repeatability and reproducibility.

For the reference standard, a working standard batch characterised against PhEur CRS for Zopiclone is used. For impurities certificates of analysis are also provided for reference standards.

Batch analyses are provided for six batches. Related substances are either given as total or as limit tests only. Elsewhere, it has been reported that no impurities A or B have found in the product.

## **6. PART IIF – STABILITY**

The drug substance stability data indicate the drug substance to be stable with acceptable total impurity levels. The applicant has stated a re-test period of 36 months and this is acceptable.

For the finished product, batches packaged in the primary pack and stored at 25°C/60%/RH real time and 40°C/75%/RH accelerated are subjected to stability. The stability protocol indicates a real time duration of 36 months.

The parameters of the finished product specification are monitored using the test methods of the FPS.

The specification includes a limit for unknown impurities that are reported in the dossier. A shelf life of 36 months at 25°C is proposed.

There is no information on an in-use shelf life for this product but this could be considered acceptable for this stable solid product.

## **7. PART IIG – BIOEQUIVALENCE / BIOAVAILABILITY**

A single dose cross over study performed in 28 adult male subjects is reported. For details the reader should refer to the clinical assessment report.

## **8. PART I – PRODUCT PARTICULARS**

### **8.1 MAA Forms**

The European MAA form is provided and is satisfactory.

### **8.2 SPC**

An SPC is provided and is satisfactory.

### **8.3 Labelling and Leaflet**

Draft black and white mock-ups are provided.

### **8.4 GMP Status**

The current manufacturing site was inspected for GMP compliance by the MHRA between 4-8 October 2004.

A wholesale dealer's licence from Belgium is provided for the MAH.

### **8.5 BSE/TSE Compliance**

Magnesium stearate is of vegetable origin. Lactose monohydrate complies with CPMP note for guidance on TSE and is already used in licensed products.

## **9. PHARMACEUTICAL EXPERT REPORT**

The expert report written by a Belgian pharmacist with little industrial experience was largely a non-critical summary and at places inadequate for its intended purpose.

## **10. PHARMACEUTICAL CONCLUSION**

A product licence should be granted for this product.

## **PRECLINICAL ASSESSMENT**

No new preclinical data have been supplied with these applications and none are required for an application of this type.



## **CLINICAL ASSESSMENT**

### **1. INTRODUCTION**

This national abridged application claims essential similarity to Zimovane 7.5 mg tablets PL 00012/0259 Aventis, first marketed 23.08.1989

### **2. BACKGROUND**

Zopiclone is a benzodiazepine hypnotic.

### **3. INDICATIONS**

Satisfactory. Consistent with originator

### **4. DOSE & DOSE SCHEDULE**

Satisfactory. Consistent with originator

### **4. TOXICOLOGY**

No new data

### **5. CLINICAL PHARMACOLOGY**

The applicant has submitted a new comparative bioequivalence study.

This was a randomised two sequence study two period two way cross-over single dose study comparing test formulation with Imovane 7.5 mg. 26 out of 28 male subjects completed the trial.

Results

Table 1

**Table 1. Summary of comparative pharmacokinetic data of zopiclone in fasting condition. Each point represents the arithmetic mean±SD (n=24).(Refer Appendix 14.2.1.3)**

PK Parameters	Test (A) Zopiclone 7.5 mg tablets Batch No.: D2334 PSI, Belgium	Reference(B) Imovane 7.5 mg tablets Batch No.: 04314 Aventis, Belgium	P-value	90% Confidence limit
C <sub>max</sub> (ng/ml)	67.869±12.05	62.669±18.27	0.0374	1.0239-1.2047
AUC(0-t) (ng.h/ml)	440.258±117.26	445.406±161.81	0.7679	0.95146-1.0733
AUC(0-inf) (ng.h/ml)	460.319±122.14	468.396±165.36	0.9971	0.94511-1.0583
T <sub>max</sub> (h)	1.229±0.86	1.794±0.91	-	-

Table 2

**Linear Plot**

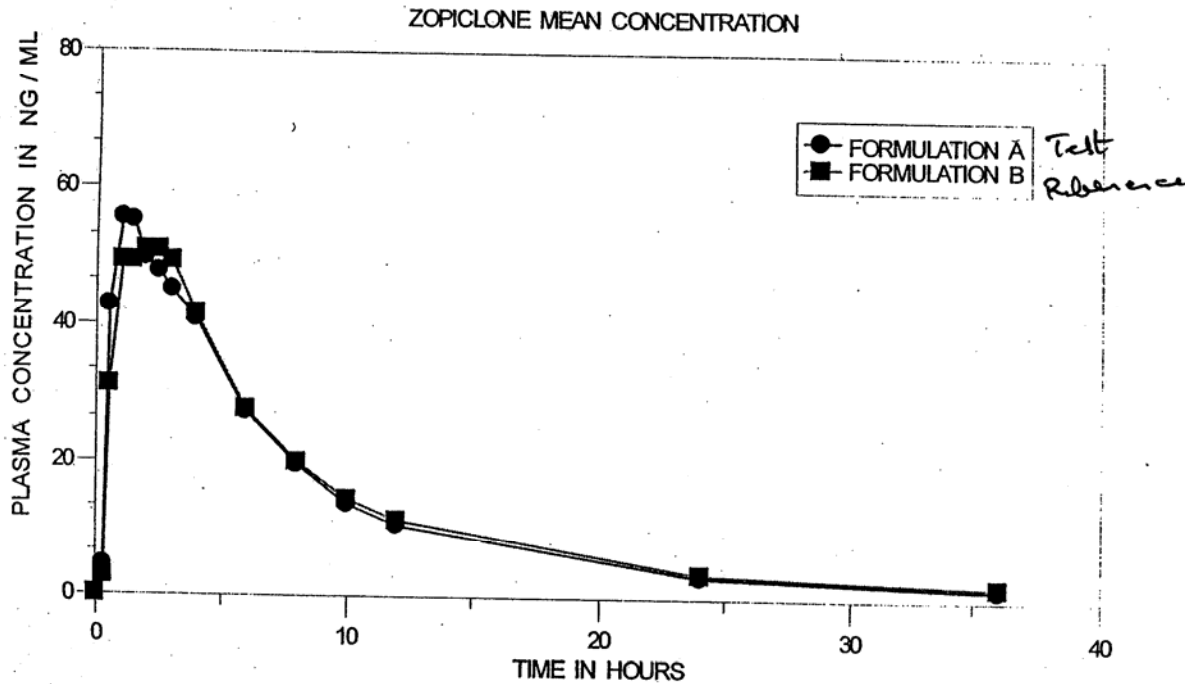


Table 3

**Table 4. Summary Table of the Main Study Results for Tests (A) and Reference (B) Of Zopiclone**

Parameter	Test (A)		Test (B)		F (treatment)	Inference	P
	Mean	CV%	Mean	CV%			
Cmax	67.869	17.8	62.669	29.1	4.90868	S	0.0374
Tmax	1.229	69.9	1.794	50.7	-	NS	-
AUC (0-t)	440.258	26.6	445.406	36.3	0.08924	NS	0.7679
AUC(0-inf.)	460.319	26.5	468.396	35.3	1.32093e-005	NS	0.9971
T1/2	6.572	16.1	6.731	25.6	0.00721	NS	0.9331

## 7. EFFICACY

No new data

## 8. SAFETY

No new data . There were no adverse events reported in the bioavailability study.

## 9. EXPERT REPORTS

The applicant has submitted an expert report by an appropriately qualified physician

## 10. PATIENT INFORMATION LEAFLET (PIL)

Satisfactory

## 11. LABELLING

Satisfactory

## 12. APPLICATION FORM (MAA)

Medically satisfactory

### **13. SUMMARY OF PRODUCT CHARACTERISTICS (SPC)**

Satisfactory. Fully consistent with originator

### **14. DISCUSSION**

The applicant has satisfactorily demonstrated comparative bioavailability of test product and the reference product Imovane a regards 90% Confidence interval ranges for AUC<sub>0-t</sub> and C<sub>max</sub>. CI for ratios test/reference AUC and C<sub>max</sub> both lay within the 80 - 125% guideline ranges.

### **15. MEDICAL CONCLUSION**

Marketing authorisation is recommended.

## **OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT**

### **QUALITY**

The important quality characteristics of Zopiclone 7.5mg film-coated Tablets are well defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

### **PRECLINICAL**

No new preclinical data were submitted and none are required for applications of this type.

### **EFFICACY**

Bioequivalence has been demonstrated between the applicant's Zopiclone 7.5mg film-coated Tablets and Zimovane 7.5mg tablets.

No new or unexpected safety concerns arise from these applications.

The SPC, PIL and labelling are satisfactory and consistent with that for Zimovane tablets.

### **RISK BENEFIT ASSESSMENT**

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The bioequivalence study supports the claim that the applicant's products and the innovator products are interchangeable. Clinical experience with zopiclone is considered to have demonstrated the therapeutic value of the compound. The risk benefit is therefore considered to be positive.

**ZOPICLONE 7.5MG FILM-COATED TABLETS (ZOPICLONE)  
PL 19156/0015**

**STEPS TAKEN FOR ASSESSMENT**

1	The MHRA received the marketing authorisation application on 15/04/2003
2	Following standard checks and communication with the applicant the MHRA considered the application valid on 05/06/2003.
3	Following assessment of the application the MHRA requested further information relating to the dossier on 19/09/2003, 19/01/2004 and again on 11/02/2005.
4	The applicant responded to the MHRA's requests, providing further information relating to the quality dossier on 25/08/2004, 22/03/2005 and 18/08/2005.
5	The application was determined on 15/12/2005.

**ZOPICLONE 7.5MG FILM-COATED TABLETS (ZOPICLONE)  
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**STEPS TAKEN AFTER ASSESSMENT**

<b>Date submitted</b>	<b>Application type</b>	<b>Scope</b>	<b>Outcome</b>

**ZOPICLONE 7.5MG FILM-COATED TABLETS (ZOPICLONE)  
PL 19156/0015**

**SUMMARY OF PRODUCT CHARACTERISTICS**

**1. NAME OF THE MEDICINAL PRODUCT**

Zopiclone 7.5 mg, film coated tablets

**2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each tablet contains 7.5 mg of zopiclone.  
For excipients, see 6.1.

**3. PHARMACEUTICAL FORM**

Film coated tablet.

**4. CLINICAL PARTICULARS**

**4.1. Therapeutic indications**

Short term treatment of insomnia, including difficulties in falling asleep, nocturnal awakening and early awakening, transient, situational or chronic insomnia, and insomnia secondary to psychiatric disturbances, in situations where the insomnia is debilitating or is causing severe distress for the patient.

Long-term continuous use is not recommended.

A course of treatment should employ the lowest effective dose.

**4.2. Posology and method of administration**

Adults:

The recommended dose is 7.5 mg zopiclone by the oral route shortly before retiring.

Elderly:

A lower dose of 3.75 mg zopiclone should be employed to start treatment in the elderly. Depending on effectiveness and acceptability, the dosage subsequently may be increased if clinically necessary.

Patients with hepatic insufficiency:



As elimination of zopiclone may be reduced in patients with hepatic dysfunction, a lower dose of 3.75 mg zopiclone nightly is recommended. The standard dose of 7.5 mg zopiclone may be used with caution in some cases, depending on effectiveness and acceptability.

Renal insufficiency:

Accumulation of zopiclone or its metabolites has not been seen during treatment of insomnia in patients with renal insufficiency. However, it is recommended that patients with impaired renal function should start treatment with 3.75 mg.

Treatment duration:

Transient insomnia: 2-5 days.

Short term insomnia: 2-3 weeks.

A single course of treatment should not continue for longer than 4 weeks including any tapering off.

Route of administration:

Oral. Each film coated tablet should be swallowed whole without sucking, chewing or breaking.

### **4.3. Contraindications**

Zopiclone 7.5 mg, film coated tablets is contraindicated in patients with myasthenia gravis, respiratory failure, severe sleep apnoea syndrome, severe hepatic insufficiency and those people with a hypersensitivity to zopiclone. As with all hypnotics Zopiclone 7.5 mg, film coated tablets should not be used in children.

### **4.4. Special warnings and precautions for use**

Use in hepatic insufficiency:

A reduced dosage is recommended, see Posology and method of administration.

Use in renal insufficiency:

A reduced dosage is recommended, see Posology and method of administration.

Risk of dependence:

Clinical experience to date with Zopiclone 7.5 mg, film coated tablets suggests that the risk of dependence is minimal when the duration of treatment is limited to not more than 4 weeks.

Use of benzodiazepines and benzodiazepine-like agents (even at therapeutic doses) may lead to the development of physical and psychological dependence upon these products. The risk of dependence increases with dose and duration of treatment; it is also greater in patients with a history of alcohol and or drug abuse, or those who have marked personality disorders. The decision to use a hypnotic in such patients should be taken only with this clearly in mind. If physical dependence has developed, abrupt termination of treatment will be accompanied by withdrawal symptoms. These may consist of headaches, muscle pain, extreme anxiety, tension,

restlessness, confusion and irritability. In severe cases the following symptoms may occur: derealisation, depersonalisation, hyperacusis, numbness and tingling of the extremities, hypersensitivity to light, noise and physical contact, hallucinations or epileptic seizures. Rare causes of abuse have been reported.

Withdrawal:

The termination of treatment with Zopiclone 7.5 mg, film coated tablets is unlikely to be associated with withdrawal effects when duration of treatment is limited to 4 weeks. Patients may benefit from tapering of the dose before discontinuation.

Depression:

As with other hypnotics, zopiclone does not constitute a treatment for depression. Any underlying cause of the insomnia should also be addressed before symptomatic treatment.

Tolerance:

Some loss of efficacy to the hypnotic effect of benzodiazepines and benzodiazepines-like agents may develop after repeated use for a few weeks. However, with Zopiclone 7.5 mg, film coated tablets there is an absence of any marked tolerance during treatment periods of up to 4 weeks.

Rebound insomnia:

Rebound insomnia is a transient syndrome where the symptoms which led to treatment with a benzodiazepine or benzodiazepine-like agent recur in an enhanced form on discontinuation of therapy. It may be accompanied by other reactions including mood changes, anxiety and restlessness. Since the risk of withdrawal/rebound phenomena may be increased after prolonged treatment, or abrupt discontinuation of therapy, decreasing the dosage in a stepwise fashion may be helpful.

A course of treatment should employ the lowest effective dose for the minimum length of time necessary for effective treatment. See Posology and method of administration for guidance on possible treatment regimen. A course of treatment should not continue for longer than 4 weeks including any tapering off.

Amnesia:

Amnesia is rare, but anterograde amnesia may occur, especially when sleep is interrupted or when retiring to bed is delayed after taking the film coated tablet. Therefore, patients should ensure that they take the film coated tablet when certain of retiring for the night and they are able to have a full night's sleep.

Driving:

It has been reported that the risk that zopiclone adversely affects driving ability is increased by the concomitant intake of alcohol. Therefore, it is recommended not to drive while taking zopiclone and alcohol concomitantly.

#### **4.5. Interactions with other medicinal products and other forms of interaction**

The sedative effect of zopiclone may be enhanced when used in combination with alcohol, concomitant use is therefore not recommended. In particular this could affect the patient's ability to drive or use machines.

In combination with CNS depressants an enhancement of the central depressive effect may occur. The therapeutic benefit of co-administration with antipsychotics (neuroleptics), hypnotics, anxiolytics/sedatives, antidepressant agents, narcotic analgesics, anti-epileptic drugs, anaesthetics and sedative antihistamines should

therefore be carefully weighed. Concomitant use of benzodiazepines or benzodiazepine-like agents with narcotic analgesics may enhance their euphoric effect and could lead to an increase in psychic dependence. Compounds which inhibit certain hepatic enzymes (particularly cytochrome P450) may enhance the activity of benzodiazepines and benzodiazepine-like agents.

The effect of erythromycin on the pharmacokinetics of zopiclone has been studied in 10 healthy subjects. The AUC of zopiclone is increased by 80% in presence of erythromycin which indicates that erythromycin can inhibit the metabolism of drugs metabolised by CYP 3A4. As a consequence, the hypnotic effect of zopiclone may be enhanced.

#### **4.6. Pregnancy and lactation**

##### Pregnancy:

Experience of use of zopiclone during pregnancy in humans is limited although there have been no adverse findings in animals. Use in pregnancy is therefore not recommended. If the product is prescribed to a woman of child bearing potential, she should be advised to contact her physician about stopping the product if she intends to become pregnant, or suspects that she is pregnant.

Moreover, if zopiclone is used during the last three months of pregnancy or during labour, due to the pharmacological action of the product, effects on the neonate, such as hypothermia, hypnotic and respiratory depression can be expected.

Infants born to mothers who took benzodiazepines or benzodiazepine-like agents chronically during the latter stages of pregnancy may have developed physical dependence and may be at some risk of developing withdrawal symptoms in the postnatal period.

##### Lactation:

Zopiclone is excreted in breast milk and use in nursing mothers must be avoided.

#### **4.7. Effects on ability to drive and use machines**

Although residual effects are rare and generally of minor significance, patients should be advised not to drive or operate machinery the day after treatment until it is established that their performance is unimpaired. The risk is increased by concomitant intake of alcohol (see Special warnings and precautions for use).

#### **4.8. Undesirable effects**

##### Nervous system disorders

Psychological and behavioural disturbances, such as irritability, aggressiveness, confusion, depressed mood, anterograde amnesia, hallucinations and nightmares have been reported. Rarely these reactions may be severe and may be more likely to occur in the elderly.

Less commonly, dizziness, headache and drowsiness have occurred.

More rarely, light headedness and incoordination have been observed.

#### Gastrointestinal disorders

Less commonly, mild gastrointestinal disturbances, including nausea and vomiting have occurred.

#### Skin and subcutaneous tissue disorders

Rarely, allergic and allied manifestations such as urticaria or rashes have been observed.

#### General disorders and administration site conditions

A mild bitter or metallic after-taste is the most frequently reported adverse effect.

Less commonly, dry mouth has occurred.

### **4.9. Overdose**

Overdose is usually manifested by varying degrees of central nervous system depression ranging from drowsiness to coma according to the quantity ingested. Overdose should not be life-threatening unless combined with other CNS depressants (including alcohol).

Symptomatic and supportive treatment in an adequate clinical environment is recommended. Attention should be paid to respiratory and cardiovascular functions. Gastric lavage is only useful when performed soon after ingestion. Haemodialysis is of no value due to the large volume of distribution of zopiclone. Flumazenil may be a useful antidote.

## **5. PHARMACOLOGICAL PROPERTIES**

Pharmacotherapeutic group: benzodiazepine related drugs

ATC code: N05CF01.

### **5.1. Pharmacodynamic properties**

Zopiclone is an hypnotic agent, and a member of the cyclopyrrolone group of compounds. It rapidly initiates and sustains sleep with reduction of total REM sleep and with preservation of slow wave sleep. Negligible residual effects are seen the following morning. Its pharmacological properties include hypnotic, sedative, anxiolytic, anticonvulsant and muscle-relaxant actions. These are related to its high affinity and specific agonist action at central receptors belonging to the “GABA”

macromolecular receptor complex modulating the opening of the chloride ion channel. However, it has been shown that zopiclone and other cyclopyrrolones act on a different site to those of benzodiazepines including different conformational changes in the receptor complex.

## 5.2. Pharmacokinetic properties

### Absorption:

Zopiclone is absorbed rapidly. Peak concentrations are reached within 1.5-2 hours and they are approximately 30 ng/ml and 60 ng/ml after administration of 3.75 mg and 7.5 mg respectively. Absorption is not modified by gender, food or repetition of doses.

### Distribution:

The product is rapidly distributed from the vascular compartment. Plasma protein binding is weak (approximately 45%) and non saturable. There is very little risk of drug interactions due to protein binding. The volume of distribution is 91.8-104.6 litres.

At doses between 3.75-15 mg, plasma clearance does not depend on dose. The elimination half life is approximately 5 hours. After repeated administration, there is no accumulation, and inter-individual variations appear to be very small.

### Metabolism:

The main metabolites are the n-oxide derivative (pharmacologically active in animals) and the n-desmethyl metabolite (pharmacologically inactive in animals). Their apparent half-lives (evaluated from the urinary data) are approximately 4.5 hours and 1.5 hours respectively. No significant accumulation is seen on repeated dosing (15 mg) for 14 days. In animals, no enzyme induction has been observed even at high doses.

### Excretion:

The low renal clearance value of unchanged zopiclone (mean 8.4 ml/min) compared with the plasma clearance (232 ml/min) indicates that zopiclone clearance is mainly metabolic. The product is eliminated by the urinary route (approximately 80%) in the form of free metabolites (n-oxide and n-desmethyl derivatives) and in the faeces (approximately 16%).

### Special patient groups:

In elderly patients, notwithstanding a slight decrease in hepatic metabolism and lengthening of elimination half-life to approximately 7 hours, various studies have shown no plasma accumulation of drug substances on repeated dosing. In renal insufficiency, no accumulation of zopiclone or of its metabolites has been detected after prolonged administration. Zopiclone crosses dialysis membranes. In cirrhotic patients, the plasma clearance of zopiclone is clearly reduced by the slowing of the desmethylation process: dosage will therefore have to be modified in these patients.

## 5.3. Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1. List of excipients**

Calcium hydrogen phosphate dihydrate  
lactose monohydrate  
maize starch  
sodium starch glycollate type A  
magnesium stearate  
hydroxypropylmethylcellulose  
propylene glycol  
titanium dioxide  
talc.

### **6.2. Incompatibilities**

None stated.

### **6.3. Shelf life**

3 years.

### **6.4. Special precautions for storage**

Do not store above 25°C.

Store in the original package.

### **6.5. Nature and contents of container**

Zopiclone 7.5 mg, film coated tablets are provided in PVC/PVdC/aluminium foil blisters containing 28 tablets.

### **6.6. Instruction for use and handling (, and disposal)**

No special instructions.

**7. MARKETING AUTHORISATION HOLDER**

PSI NV  
Kraanlei 27  
B-9000 Ghent  
Belgium

**8. MARKETING AUTHORISATION NUMBER**

PL 19156/0015

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

15/12/2005

**10. DATE OF REVISION OF THE TEXT**

# ZOPICLONE 7.5MG FILM-COATED TABLETS (ZOPICLONE) PL 19156/0015

## PRODUCT INFORMATION LEAFLET

### PATIENT INFORMATION LEAFLET

Read all of this leaflet carefully before you start taking this medicine.

- *Keep this leaflet. You may need to read it again.*
- *If you have further questions, please ask your doctor or your pharmacist.*
- *This medicine has been prescribed for your personally and you should not pass it on to others. It may harm them, even if their symptoms are the same as yours.*

#### *In this leaflet*

1. What Zopiclone film coated tablets is and what it is used for?
2. Before you take Zopiclone film coated tablets
3. How to take Zopiclone film coated tablets?
4. Possible side effects
5. Storing Zopiclone film coated tablets

#### Zopiclone 7.5 mg, film coated tablets

- *The active substance* is zopiclone.
- *The other ingredients* are calcium hydrogen phosphate dihydrate, lactose monohydrate, maize starch, sodium starch glycolate type A, magnesium stearate, hydroxypropylmethylcellulose, propylene glycol, titanium dioxide, talc

#### Marketing authorisation holder

PSI NV  
Kraanlei 27  
B-9000 Ghent  
Belgium

#### Manufacturer

Kela Laboratoria NV  
St. Lenaartseweg 48  
B-2320 Hoogstraten  
Belgium

#### Product licence number

PL 19156/0015

### 1. WHAT ZOPICLONE 7.5 MG, FILM COATED TABLETS IS AND WHAT IS IT USED FOR?

- Film coated tablet.  
Each film coated tablet contains 7.5 mg of zopiclone. Zopiclone is one of a group of medicines called hypnotics. It should help you to sleep, without leaving you feeling drowsy the next day.
- The film coated tablets come in a pack of 28 tablets but your doctor will prescribe as many as your need.
- These film coated tablets are normally used for the short-term treatment of severe sleeping difficulties. If you need any further information on your condition, please ask your doctor.

### 2. BEFORE YOU TAKE ZOPICLONE 7.5 MG, FILM COATED TABLETS

#### Do not take Zopiclone 7.5, film coated tablets

- If you are sensitive to or allergic to zopiclone or any of the inactive ingredients.
- If you suffer from myasthenia gravis (a condition where the muscles easily tire and become weak).
- If you have any breathing problems, especially during sleep.
- If you have any liver or kidney problems.
- If the patient is under 12 years of age.

#### Take special care with Zopiclone 7.5 mg, film coated tablets

- If you have a personality disorder.
- If you have ever been treated for drug or alcohol abuse.
- Do not break the film coated tablets.
- If you are taking any medicines belonging to the hypnotic group there is a possibility that you may become dependent on them. However, with Zopiclone 7.5 mg, film coated tablets this possibility is small.
- Alcohol can affect the way Zopiclone 7.5 mg, film coated tablets works, you should not drink alcohol whilst taking these film coated tablets.

#### Pregnancy

Tell your doctor or pharmacist if you are pregnant or think you might be pregnant.

If your doctor has prescribed Zopiclone 7.5 mg, film coated tablets during the later stages of pregnancy then there may be some effects on the baby when it is born. Tell your doctor or midwife that you have taken Zopiclone 7.5 mg, film coated tablets.

Ask your doctor or pharmacist for advice before taking any medicine.

#### Breast-feeding

Tell your doctor or pharmacist if you are breast-feeding.

Ask your doctor or pharmacist for advice before taking any medicine.

#### Driving and using machines

- You should not drive if you drink alcohol whilst taking Zopiclone 7.5 mg, film coated tablets.
- Rarely the film coated tablets may cause daytime drowsiness. You should not drive or operate machinery unless you are sure that you are not affected.

#### Taking other medicines

'Please note that these statements may also apply to products used some time ago or at some time in the future.'

'Please inform your doctor or pharmacist if you are taking, or have recently taken, any other medicine – even those not prescribed.'



- If you are taking any other medicines, these medicines may change the way your zopiclone film coated tablets work e.g. any other treatment to help you sleep, any treatment for schizophrenia and psychotic disorders, any other treatment for anxiety or depression, any treatment for epilepsy, any strong pain killers such as codeine, morphine, or diamorphine, sedative antihistamines (to treat allergies, skin irritation or vomiting) or erythromycin (an antibiotic to treat infections).

If you have to go to a doctor, dentist or hospital for any reason, tell them that you are taking Zopiclone 7.5 mg, film coated tablets.

### 3. HOW TO TAKE ZOPICLONE 7.5 MG, FILM COATED TABLETS?

- Your doctor will have told you how much to take. The number of the film coated tablets you need to take will depend on your condition. The usual adult dosage is one Zopiclone 7.5 mg, film coated tablet. Your treatment will usually be for less than four weeks, and the doctor may reduce your dose near the end of your course.
- For elderly patients and people with liver or kidney problems, the starting dosage is usually  $\frac{1}{2}$  Zopiclone 7.5 mg film coated tablet. The film coated tablets should be swallowed whole with a small glass of water shortly before retiring.
- These film coated tablets are not recommended for children.

*If you have the impression that the effect of Zopiclone 7.5 mg, film coated tablets is too strong or too weak talk to your doctor or pharmacist.*

#### **If you take more Zopiclone 7.5 mg, film coated tablets than you should**

*If you may have taken more Zopiclone 7.5 mg, film coated tablets than you should, talk to a doctor or pharmacist immediately.*

#### **If you forget to take Zopiclone 7.5 mg, film coated tablets?**

*Do not take a double dose to make up for forgotten individual doses*

Do not worry, just take your next film coated tablet at the usual time, then go on as before.

#### **Effects when treatment with Zopiclone 7.5 mg, film coated tablets is stopped**

The termination of treatment with Zopiclone 7.5 mg, film coated tablets is unlikely to be associated with withdrawal effects when duration of treatment is limited to 4 weeks. Patients may benefit from tapering of the dose before discontinuation.

### 4. POSSIBLE SIDE EFFECTS

*Like all medicines, Zopiclone 7.5 mg, film coated tablets can have side effects.*

- Nervous system disorder  
Mood changes such as irritability or aggressiveness, confusion, depression, loss of memory, hallucinations and nightmares have been reported.  
Less commonly, dizziness, headache and drowsiness have occurred.  
More rarely, light headedness and loss of coordination have been observed.
- Respiratory, thoracic and mediastinal disorder  
Difficulty in breathing.
- Gastrointestinal disorders  
Less commonly, mild stomach discomfort, nausea and vomiting have been observed.
- Skin and subcutaneous tissue disorders  
Rarely, skin rashes with or without itching.
- General disorders and administration site conditions  
A mild bitter or metallic taste in the mouth is the most frequently reported adverse effect.  
Less commonly, dry mouth has occurred.

Do not be alarmed by this list of possible events. Most people take Zopiclone 7.5 mg, film coated tablets without any problems.

*If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.*

### 5. STORING ZOPICLONE 7.5 MG, FILM COATED TABLETS

*Keep all medicines out of the reach and sight of children.*

Do not store above 25°C.  
Store in the original package.

*You must not take these tablets after the expiry date. This is given in two places:*  
- on the carton  
- on the blister

*In both places it is given as "EXP" followed by the month and year. The tablets should not be used after the end of that month. If you are not sure when this is, check with your doctor or pharmacist.*

Do not keep the tablets if your doctor decides to stop treatment. Return them to your pharmacist who will arrange for their safe destruction.

*This leaflet was approved .....*

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**ZOPICLONE 7.5MG FILM-COATED TABLETS (ZOPICLONE)  
PL 19156/0015**

**LABELLING**

